UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,989	02/01/2006	Navin Vaya	4062-158	4603

23117 7590 10/10/2006

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
MERCIER, MELISSA S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/522,989	VAYA ET AL.	
	Examiner	Art Unit	
	Melissa S. Mercier	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-74* is/are rejected.

7)☒ Claim(s) *12,13,44,45,61 and 70* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-74 are pending in this application. Claims 1-74 are rejected.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 70 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must be in the alternative. Claim 70 is dependent on claims 60 and 68. See MPEP § 608.01(n). Accordingly, the claim 70 not been further treated on the merits.

Claims 12-13 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 4-5. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 44-45 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 36-37. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 61 objected to as being dependent upon a rejected base claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 1 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant uses the limitation "comprising a duel retard technique to control the release". It is unclear to the examiner what applicant is claiming with this limitation. Applicant has not provided a definition or a basis for the examiner to determine the definition. Claims 2-29, and 33-72 are included in this rejection, since they depend on Claims 1 and 33.

Claims 3 and 35 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear to the examiner what the applicant intends to claim with the limitation of "with sufficient reduction", applicant does not explain or offer direction as to the scope of sufficient reduction would comprise.

Claim 3 recites the limitation "the amount of release controlling agent" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 1, to which claim 3 depends does not contain a release-controlling agent.

Regarding claims 5, 13, 37, and 45 the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claims 6 and 38, the phrase "selected preferably from" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). It is unclear to the examiner what hydrophobic release controlling agents applicant is claiming.

Regarding claims 7 and 39, the phrase "wherein the preferred ammonio methoacrylate co-polymer are selected from" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Further regarding Claims 7 and 39, the use of the trademark Eudragit RSPO, Eudragit RL, and Eudragit NE30D has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claims 9-11, 41-43, 49-50 and 64-65 are further rejected under 35 U.S.C. 112, second paragraph, the phrases "preferably, more preferably, and most preferably"

renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 28 recites the broad recitation can be given twice a day, and the claim also recites preferably can be given once a day which is the narrower statement of the range/limitation.

Claims 30 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: related to how the preparation of the inner and outer portions of the tablet is to be performed. The claim does not provide any means of making the tablet. It is unclear to the examiner how one of ordinary skill in the art would know how to prepare such tablet.

Claims 63-67 recites the limitation "the maximum plasma metformin concentration, the modified release metformin hydrochloride formulations, and the minimum plasma metformin concentration" in line 2. There is insufficient antecedent basis for this limitation in the claim. There is no antecedent basis for the metformin concentration in the claims to which 63-67 depends.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 21-22, and 24-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

Glassman teaches, "a super-fast-starting, slow release medicinal tablet, wherein the tablet is comprised of two layers of compressed matrix that are fused together by means of a readily dissolvable adhesive substance, and in which one of the layers is a lightly compressed top layer containing a pure unadulterated, uncoated, active drug and which has one or more radial grooves in it's top surface to enhance rapid breakdown of the tablet; and the other layer has a strongly compressed portion comprised of a medically inert or inactive matrix having

embedded throughout a multitude of pellets, each containing an active ingredient and having enteric coatings of various thicknesses so as to variably delay disintegration of the pellets" (abstract).

Glassman does not teach the pharmaceutical active as being highly soluble, the immediate release portion being a low dose, or the modified release being a high dose.

Paradissis teaches, "formulations composed of a mixture of 0 to 50% of an immediate release particle containing a core of drug, inert spherical substrate particles and binder, coated with talc and up to 100% of an extended release particle comprising the immediate release particle coated with a dissolution modifying system containing plasticizers and a film forming agent, wherein the particle size of the extended release formulation is -10+60 mesh" (column 3, lines 21-33). The Examiner is interpreting the particle stated particle size for the extended release particles to include the coating; therefore the coating would be a micro matrix.

While the Paradissis patent does not specifically teach that the pharmaceutical actives must be highly soluble, it does teach, "a wide variety of medicaments which are orally administered as tablets maybe used, these include acetaminophen, which applicant provides as one example of a highly soluble active. "The drugs used in the formulations of Paradissis may be selected from a wide variety of pharmaceutical formulations with particular pharmaceutical compounds being analgesics, anti-inflammatories, antihistamines, antitussives, expectorants, decongestants, narcotics, antibiotics, bronchodilators, cardiovasculars, central nervous system (CNS) drugs, metal salts, minerals, vitamins and mixtures thereof" (column 3, lines 34-41).

Further it would be obvious to one of ordinary skill in the art to substitute any active pharmaceutical into the teachings of Glassman and Paradissis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Webb et al. (US Patent 4,996 061).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Glassman and Paradissis do not teach a tablet, in which the inner portion is covered by the outer portion from all sides except the top surface that remains uncovered.

Webb teaches, "a variation of the compression-coated tablet is the inlay tablet, also referred to as a dot, or bull's-eye tablet. Instead of an inner core zone

being completely surrounded by an outer coat, one surface of the zone corresponding to an inner core zone is exposed. These tablets have at least two discrete zones of granulation compressed together, i.e., an inlay zone and a base zone. The preparation of inlay tablets is similar to the preparation of compression-coated tablets except that a surface of coating is eliminated" (column 6, lines 3-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman and Paradissis with the tablet of Webb in order to provide sustained-release of an active pharmacueitcal with immediate release of another or the same active pharmaceutical.

Claims 1, and 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Paradissis teaches, "water-insoluble hydrophobic agents, such as diethyl phthalate, diethyl sebacate and castor oil are used to delay the release of water-soluble drugs, such as potassium chloride" (column 6, lines48-52) and "the film forming agents, which are also preferably employed in a spraying solution along with the plasticizer, may be selected from a wide variety of film forming materials. Preferable materials, however, may be selected from the group consisting of acrylic and

methacrylic acid copolymers and cellulose derivatives. Exemplary cellulose derivatives include ethylcellulose, methylcellulose, cellulose acetate, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose and mixtures thereof" (column 7, lines 4-13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Claims 1, 4-7, and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and further in view of Lerner et al. (US Patent 5,840,332).

The teachings of Glassman and Paradissis as they apply to claim 1 are described above and applied in the same manner.

Lerner teaches, "a gastrointestinal delivery system is provided. The system comprises a drug in combination with a core material, the core being surrounded by a water-insoluble or relatively water-insoluble coating material in which

particulate water-insoluble material is embedded. When the delivery device enters the gastrointestinal tract, the particulate matter takes up liquid, thus forming channels interconnecting the drug-containing core with the outside of the delivery device. These channels allow the release of drug from the core into the gastrointestinal tract. By controlling parameters in the device, such as the core material, carrier material in the coating, and particulate matter, the location of release of the drug can be carefully controlled" (abstract).

Additionally, Lerner teaches, "the coating includes, but is not limited to, any combination of a water-insoluble polysaccharide, water-insoluble crosslinked polysaccharide, a water-insoluble polysaccharide metal salt, a water-insoluble crosslinked protein or peptide, a water-insoluble crosslinked hydrophilic polymer in a dried powder form as the particulate and any hydrophobic polymer coating known in the art as the water-insoluble carrier. Specific examples of the water-insoluble carrier include, but are not limited to, Eudragit E.TM., Eudragit NE.TM., Eudragit RL.TM., Eudragit RS.TM., ethylcellulose, shellac, zein, and waxes" (column 9, lines 38-65).

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components

of coating materials used in pharmaceutical compositions. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 1, 8-11, and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Additionally, Paradissis teaches, "the extended release particles of the invention are then prepared by taking the immediate release particles and coating them with a dissolution modifying system which functions as a diffusion membrane around the coated core. The dissolution modifying system contains a plasticizer and a film forming agent which is applied by spraying the immediate release particles with about 2 to about 35% by weight of the dissolution modifying system coating. The dissolution modifying system is designed to encapsulate the particles and modify the drugs dissolution profile so that a sustained/extended drug release rate is obtained. In other words, the system is formulated to each drug profile to permit a release of the drug from the particles over a 12 to at least 24 hour period (column 6, lines 32-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the percentages of coating on the micro matrix particles in order to provide the release of the modified release component that was desired.

Claims 1 and 14-15 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Paradissis additionally teaches, "preferred plasticizers may be selected from the group consisting of diethyl phthalate, diethyl sebacate, triethyl citrate, crotonic acid, propylene glycol, butyl phthalate, dibutyl sebacate, castor oil and mixtures thereof" (column 6, lines 46-50).

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of coating materials used in pharmaceutical compositions. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 1, 19-20, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Paradissis teaches, "formulations composed of a mixture of 0 to 50% of an immediate release particle containing a core of drug, inert spherical substrate particles and binder, coated with talc and up to 100% of an extended release particle comprising the immediate release particle" (column 3, lines 21-29).

While Paradissis does not teach the exact ratios of immediate release to modified release, it would be obvious to one of ordinary skill in this art to expand upon Paradissis to arrive at the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time.

Claims 1, 26, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Paradissis further teaches as a preferred embodiment "the formulation comprises from 0 to 50% of an immediate release particle containing a core of at least one drug, and up to 100% of an extended release particle which comprises the

immediate release particle, additionally coated with a dissolution modifying system and optionally additional drug (column 3, lines 66-69, column 4, lines 1-4).

It would have been obvious to one of ordinary skill in the art that the time the invention was made to combine additional active ingredients to the tablet in order "to reduce the minimum daily number of doses from which the drug is uniformly released over a desired extended period of time" (column 1, lines 30-33).

Claims 1 and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Additionally, Paradissis teaches, "the rate of release of the pharmaceutical formulation may be described according to standardized dissolution testing procedures as found in the U.S. Pharmacopoeia XXII, where less than 50% of the drug is released within 1 hour of measurement and not less than 70% of the drug is released at the targeted dosing period, such as a 12 to at least 24-hour period (column 6, lines 39-45). It is the Examiners position that Paradissis target dosing period includes the 6-hour dosing period of the instant application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the coating thicknesses and particle sizes in order to make a dosage unit which will meet the release profile sought. One of ordinary skill in this art would be able to modify release profiles without undue experimentation.

Claims 1 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner.

Regarding Claim 28, Glassman teaches his "super-fast-acting, slow release tablet is capable of rapidly and predictably entering the Therapeutic Zone. The herein disclosed super-fast-acting, slow-release tablet (S/R) predictably enters into the Therapeutic Zone in the shortest possible time (less than one hour). That is 4-5 times faster than any known sustained release tablet, and it offers immediate and lasting therapeutic relief covering a period of 12 or more hours (column 4, lines 48-57). The Examiner is interpreting the 12 hours or more to be twice a day dosing.

Regarding Claim 29, Glassman teaches a study on asthmatic children who where given single dosages of uncoated tablets of Theophylline, which was not absorbed fast enough and therefore invented his tablet which combined uncoated and coated tablets. (column 4, lines 58-68). Therefore, it would be obvious to assume that Glassman intends his dosage forms to be used by human beings.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily

doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Claim 33, 55-57, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman and Paradissis as they apply to Claim 1 are described above and applied in the same manner. Claim 1 is drawn to a generic form of the same dosage form as claimed in the instant claim.

Glassman and Paradissis do not specifically teach the use of an antidiabetic ingredient as an active.

Timmins teaches "a biphasic controlled release delivery system for pharmaceuticals which have high water solubility, such as the antidiabetic metformin HCl salt, which includes a dosage form that has prolonged gastric residence so that a dosing regimen of at least one gram metformin, preferably 1-3 grams, once daily, may be achieved while providing effective control of plasma glucose" (abstract).

Timmins further teaches, "metformin is an antihyperglycemic agent of the biguanide class used in the treatment of non-insulin dependent diabetes mellitus

(NIDDM). It is usually marketed in the form of its hydrochloride salt as Glucophage" (column 1,lines 22-25).

While the Paradissis patent does not specifically teach that the pharmaceutical actives must be highly soluble, it does teach, "a wide variety of medicaments which are orally administered as tablets maybe used, these include acetaminophen, which applicant provides as one example of a highly soluble active. "The drugs used in the formulations of Paradissis may be selected from a wide variety of pharmaceutical formulations with particular pharmaceutical compounds being analgesics, anti-inflammatories, antihistamines, antitussives, expectorants, decongestants, narcotics, antibiotics, bronchodilators, cardiovasculars, central nervous system (CNS) drugs, metal salts, minerals, vitamins and mixtures thereof" (column 3, lines 34-41).

Further it would be obvious to one of ordinary skill in the art to substitute any active pharmaceutical into the teachings of Glassman and Paradissis.

Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829), Timmins et al. (US Patent 6,475,521), and Webb et al. (US Patent 4,996 061).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Glassman, Paradissis and Timmins do not teach a tablet, in which the inner portion is covered by the outer portion from all sides except the top surface that remains uncovered.

Webb teaches, "a variation of the compression-coated tablet is the inlay tablet, also referred to as a dot, or bull's-eye tablet. Instead of an inner core zone being completely surrounded by an outer coat, one surface of the zone corresponding to an inner core zone is exposed. These tablets have at least two discrete zones of granulation compressed together, i.e., an inlay zone and a base zone. The preparation of inlay tablets is similar to the preparation of compression-coated tablets except that a surface of coating is eliminated" (column 6, lines 3-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman, Paradissis and Timmins with the tablet of Webb in order to provide sustained-release of an active pharmaceutical with immediate release of another or the same active pharmaceutical

Claims 33, 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Paradissis teaches, "water-insoluble hydrophobic agents, such as diethyl phthalate, diethyl sebacate and castor oil are used to delay the release of water-soluble drugs, such as potassium chloride" (column 6, lines48-52) and "the film forming agents, which are also preferably employed in a spraying solution along with the plasticizer, may be selected from a wide variety of film forming materials. Preferable materials, however, may be selected from the group consisting of acrylic and methacrylic acid copolymers and cellulose derivatives. Exemplary cellulose derivatives include ethylcellulose, methylcellulose, cellulose acetate, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose and mixtures thereof" (column 7, lines 4-13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Claims 33, 36-39, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US

Patent 5,445,829), Timmins et al. (US Patent 6,475,521), and further in view of Lerner et al. (US Patent 5,840,332).

The teachings of Glassman and Paradissis as they apply to claim 33 are described above and applied in the same manner.

Lerner teaches, "a gastrointestinal delivery system is provided. The system comprises a drug in combination with a core material, the core being surrounded by a water-insoluble or relatively water-insoluble coating material in which particulate water-insoluble material is embedded. When the delivery device enters the gastrointestinal tract, the particulate matter takes up liquid, thus forming channels interconnecting the drug-containing core with the outside of the delivery device. These channels allow the release of drug from the core into the gastrointestinal tract. By controlling parameters in the device, such as the core material, carrier material in the coating, and particulate matter, the location of release of the drug can be carefully controlled" (abstract).

Additionally, Lerner teaches, "the coating includes, but is not limited to, any combination of a water-insoluble polysaccharide, water-insoluble crosslinked polysaccharide, a water-insoluble polysaccharide metal salt, a water-insoluble crosslinked protein or peptide, a water-insoluble crosslinked hydrophilic polymer in a dried powder form as the particulate and any hydrophobic polymer coating known in the art as the water-insoluble carrier. Specific examples of the water-insoluble carrier include, but are not limited to, Eudragit E.TM., Eudragit NE.TM., Eudragit RL.TM., Eudragit RS.TM., ethylcellulose, shellac,

zein, and waxes" (column 9, lines 38-65).

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of coating materials used in pharmaceutical compositions. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 33, 40-43, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829), and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to claim 33 are described above and applied in the same manner.

Additionally, Paradissis teaches, "the extended release particles of the invention are then prepared by taking the immediate release particles and coating them with a dissolution modifying system which functions as a diffusion membrane around the coated core. The dissolution modifying system contains a plasticizer and a film forming agent which is applied by spraying the immediate release particles with

about 2 to about 35% by weight of the dissolution modifying system coating. The dissolution modifying system is designed to encapsulate the particles and modify the drugs dissolution profile so that a sustained/extended drug release rate is obtained. In other words, the system is formulated to each drug profile to permit a release of the drug from the particles over a 12 to at least 24 hour period (column 6, lines 32-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the percentages of coating on the micro matrix particles in order to provide the release of the modified release component that was desired.

Claims 33, 51-52 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829), and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Paradissis teaches, "formulations composed of a mixture of 0 to 50% of an immediate release particle containing a core of drug, inert spherical substrate particles and binder, coated with talc and up to 100% of an extended release particle comprising the immediate release particle" (column 3, lines 21-29).

While Paradissis does not teach the exact ratios of immediate release to modified release, it would be obvious to one of ordinary skill in this art to expand upon Paradissis to arrive at the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time.

Claims 33 and 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Paradissis additionally teaches, "preferred plasticizers may be selected from the group consisting of diethyl phthalate, diethyl sebacate, triethyl citrate, crotonic acid, propylene glycol,butyl phthalate, dibutyl sebacate, castor oil and mixtures thereof" (column 6, lines 46-50).

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of coating materials used in pharmaceutical compositions. It therefore follows that the

instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claim 33 and 53-54 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Timmins teaches, "the use of the metformin or salt thereof in combination with another anti-hyperglycemic agent produces antihyperglycemic results greater than that possible from each of these medicaments alone and greater than the combined additive anti-hyperglycemic effects produced by these medicaments. In addition, in accordance with the present invention a method is provided for lowering insulin resistance or treating hyperglycemia including type 2 diabetes (NIDDM) and/or type 1 diabetes (IDDM) wherein a therapeutically effective amount of the biphasic formulation of the invention containing metformin or a salt thereof, optionally in combination with another antihyperglycemic agent and/or a hypolipidemic agent, is administered to a patient in need of treatment. The other antihyperglycemic agent may be an oral antihyperglycemic agent preferably a sulfonyl urea such as glyburide (also known as glibenclamide), glimepiride (disclosed in U.S. Pat. No. 4,379,785), glipizide, gliclazide or chlorpropamide, other known sulfonylureas or other antihyperglycemic agents which act on the ATP-dependent channel of the .beta.-cells, with glyburide

being preferred" (column 12, lines 38-54).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time.

Claims 33 and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis, and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Regarding Claim 58, Glassman teaches his "super-fast-acting, slow release tablet is capable of rapidly and predictably entering the Therapeutic Zone. The herein disclosed super-fast-acting, slow-release tablet (S/R) predictably enters into the Therapeutic Zone in the shortest possible time (less than one hour). That is 4-5 times faster than any known sustained release tablet, and it offers immediate and lasting therapeutic relief covering a period of 12 or more hours (column 4, lines 48-57). The Examiner is interpreting the 12 hours or more to be twice a day dosing.

Regarding Claim 59, Glassman teaches a study on asthmatic children who where given single dosages of uncoated tablets of Theophylline, which was not absorbed fast enough and therefore invented his tablet which combined uncoated and coated tablets. (column 4, lines 58-68). Therefore, it would be obvious to assume that Glassman intends his dosage forms to be used by human beings.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Claims 33 and 62 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Timmins's examples 1-3 provide dissolution profiles in which 33.1-38.1% of metformin was released at 1 hour, 57.5-79.7% was released at 4 hours, and 88.6-100% was released at 10 hours. (column 21-22). While a 12-hour time interval was not provided by, the profile parameters are met by 10 hours, therefore, they would inherently be met at 12 hours.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the percentages of coating on the micro matrix particles in order to provide the release of the modified release component that was desired.

Claims 33, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Timmons's Example 5 provides a table comparing Timmins's formulation of example 3 vs Glucophage. Timmins's Example 3 provides a Cmax (ng/mL) of 978, while Glucophage provides a Cmax of 1226. Glucophage is a commercially marketed product, which has been proven to be therapetucialy effective. Therefore, it would be obvious to one of ordinary skill in the art to make to prepare a dosage form, which would provide the equivalent parameters.

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of materials used in pharmaceutical compositions. It therefore follows that the instant

claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 33 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Additionally, Paradissis teaches, "the rate of release of the pharmaceutical formulation may be described according to standardized dissolution testing procedures as found in the U.S. Pharmacopoeia XXII, where less than 50% of the drug is released within 1 hour of measurement and not less than 70% of the drug is released at the targeted dosing period, such as a 12 to at least 24-hour period (column 6, lines 39-45). It is the Examiners position that Paradissis's target dosing period includes the 6-hour dosing period of the instant application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the coating thicknesses and particle sizes in order to make a dosage unit which will meet the release profile sought. One of ordinary skill in this art would be able to modify release profiles without undue experimentation.

Claims 33 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Timmins further teaches, "a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix or surrounding it with a polymeric barrier membrane through which drug must diffuse to be released for absorption. To reduce the rate of release of drug from the dosage form to an appropriate level consistent with the blood level profile desired for a drug possessing very high water solubility, very large amounts of polymer would be required for the matrix or barrier membrane" (column 2, lines 15-30).

Therefore, it would be obvious to one of ordinary skill in the art to make to prepare a dosage form, which would provide the equivalent parameters.

Claims 33 and 68-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

While the Paradissis patent does not specifically teach that the pharmaceutical actives must be highly soluble, it does teach, "a wide variety of medicaments which are

orally administered as tablets maybe used, these include acetaminophen, which applicant provides as one example of a highly soluble active. "The drugs used in the formulations of Paradissis may be selected from a wide variety of pharmaceutical formulations with particular pharmaceutical compounds being analgesics, anti-inflammatories, antihistamines, antitussives, expectorants, decongestants, narcotics, antibiotics, bronchodilators, cardiovasculars, central nervous system (CNS) drugs, metal salts, minerals, vitamins and mixtures thereof" (column 3, lines 34-41).

Further it would be obvious to one of ordinary skill in the art to substitute any active pharmaceutical into the teachings of Glassman, Paradissis, and Timmins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time" (Paradissis, column 1, lines 28-35).

Claims 33 and 71-72 rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Timmins et al. (US Patent 6,475,521).

The teachings of Glassman, Paradissis and Timmins as they apply to Claim 33 are described above and applied in the same manner.

Paradissis further teaches as a preferred embodiment "the formulation comprises from 0 to 50% of an immediate release particle containing a core of at least one drug,

and up to 100% of an extended release particle which comprises the immediate release particle, additionally coated with a dissolution modifying system and optionally additional drug (column 3, lines 66-69, column 4, lines 1-4).

It would have been obvious to one of ordinary skill in the art that the time the invention was made to combine additional active ingredients to the tablet in order "to reduce the minimum daily number of doses from which the drug is uniformly released over a desired extended period of time" (column 1, lines 30-33).

Claims 30-31 and 73-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829), Timmins et al. (US Patent 6,475,521).

The teaching of Glassman, Paradissis and Timmins as they relate to the tablets claimed in claims 1 and 33 are discussed above and applied in the same manner.

Timmins additionally teaches, his biphasic controlled release delivery system of the invention is a heterogeneous two phase system which includes (1) an inner solid particulate phase in the form of individual granules or particles containing (a) drug which has a high water solubility, preferably, metformin or a salt thereof, and a limited window of absorption (such as in the upper gastrointestinal tract), and (b) an extended release material formed of one or more hydrophilic polymers, and/or one or more hydrophobic polymers, and/or one or more other type hydrophobic materials (such as one or more waxes, fatty alcohols and/or fatty acid esters), and (2) an outer solid continuous phase in which granules or particles of inner solid particulate phase are dispersed and

embedded, the outer solid continuous phase which primarily is formed of an extended release material formed of one or more hydrophilic polymers, and/or one or more hydrophobic polymers, and/or one or more other type hydrophobic materials (such as one or more waxes, fatty alcohols and/or fatty acid esters) (column 8, lines 29-47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Glassman and Paradissis with the teachings of Timmins in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35) with the method of preparing such a tablet as described by Timmins.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ting et al. (US Patent 6,372,254), Conte et al. (US Patent 5,738,874), Beringer et al. (US Patent 4,139,589), and Lee et al. (PG Pub 2004/0156902).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-19, 21 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-19, 22 of copending Application No. 11/134633. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-74 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-29 and 32-72 of copending Application No. 10/630,446. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa S. Mercier whose telephone number is (571) 272-9039. The examiner can normally be reached on 7:30am-4pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MSMercier

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600